

EXHIBIT B

**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION**

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
THIS DOCUMENT RELATES TO: <i>Wave 4 Cases</i>	

EXPERT REPORT OF JOHN R. WAGNER, M.D.

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Gynecare TVT Products

I have prepared this Expert Report in the matter of In re: Ethicon, Inc. Pelvic Repair System Products Liability Litigation, MDL No. 2327, currently pending in the United States District Court for the Southern District of West Virginia, before the Hon. Joseph R. Goodwin.

I. QUALIFICATIONS AND EXPERIENCE

A *curriculum vitae* providing the details of my education, experience and training is attached as Exhibit A to this report.

I am originally from St. Louis, MO. I attended Georgetown University for my undergraduate education, where I received a Bachelor of Arts degree in Political Science in 1983. I attended medical school at Mount Sinai School of Medicine, in New York and graduated in 1987.

I completed my internship and residency from 1987-1991 at University Hospital at Stony Brook. I was the Chief Resident in 1991. In my residency, I was trained in multiple urogynecologic procedures. I trained under Jim Droesch at University Hospital Stony Brook from 1987 to 1991. During that time, he initiated the Department of Surgical Gynecology which was a large surgical referral service for benign gynecologic conditions. We performed our own urodynamic studies on an out-patient basis. We performed our own cystoscopies on an out-patient basis. I performed many surgeries for incontinence including Kelly plications, needle suspension procedures (such as the Stamey and Pereyra operations), Burch procedures, MMK's, and autologous vaginal slings. I performed many pelvic support procedures including paravaginal

repairs as well as traditional bladder suspensions. We performed multiple vaginal and abdominal operations for apical vaginal prolapse. These included sacrocolpopexy, multiple different types of culodoplasties, sacrospinous fixation, and high uterosacral ligament suspension.

At the time I worked at Stony Brook, there were very few national fellowships available in either minimally invasive surgery or urogynecology. Urogynecology is now recognized subspecialty, and I took and passed my Female Pelvic Medicine and Reconstructive Surgery boards in 2014. I have been Board Certified in OB/GYN since 1993.

For the past 25 years, I have worked in the same private practice, now called WGM Obstetrics & Gynecology. While my partner and I do practice obstetrics, our primary focus is surgical gynecology for benign conditions. Approximately half of the operations we perform are related to a minimally invasive surgical approach for large pelvic pathology. The other half is primarily related to pelvic prolapse incontinence surgery. I am one of the few surgeons nationwide that utilizes a robotic single site approach to treat pelvic organ prolapse. I routinely perform robotic single site sacrocolpopexies and vaginal and/or uterine suspension procedures. I have a large volume of patients who suffer from stress incontinence and urge incontinence. I perform my own urodynamic studies in the office. My typical incontinence procedures utilize suburethral slings.

As regards teaching positions, I am currently a Clinical Associate Professor at Hofstra University School of Medicine. My partner and I serve as co-directors for the Department of Minimally Invasive Gynecology at Huntington Hospital. We are both currently employed as “at large educators” by three different university hospitals. There are currently four different OB/GYN residencies on Long Island. Three of these also have fellowship programs in

minimally invasive gynecology and/or urogynecology. We currently are actively involved in the teaching of senior residents and fellows from all of these programs.

The residents and fellows that I operate with are exposed to vaginal mesh repairs, abdominal mesh repairs and various forms of suburethral slings. The slings I utilize are primarily those made by Johnson & Johnson (and included the TVT-Exact, TVT Abbrevio, and TVT-O). I also performed the “Classic” TVT Retropubic for many years, and used TVT Secur extensively while it was on the market.

I routinely use the IFU’s as part of my resident education. I found that these provide the best description of the current product, its use, potential complications and warnings. I encourage my residents, when they are first exposed to these products, to take the IFU’s home with them and to review them thoroughly.

When I first started in private practice, I performed Burch procedures on a regular basis. My two primary incontinence procedures were the Burch and the Pereyra needle suspension procedure. The Pereyra was less invasive, but had a significantly higher long term failure rate. The Burch procedure was more invasive but had a better long term result. Typically, a Burch procedure would require a 3-7 day hospitalization.

When the TVT became available, it revolutionized the treatment of stress incontinence. TVT provided long term outcomes equivalent to or better than the Burch procedure combined with a minimally invasive approach that was consistent with the needle suspension procedures. The landscape for treating stress incontinence was literally changed almost overnight. The

suburethral slings have so changed the treatment of SUI that there are urogynecologic fellows in today's world who graduate without ever seeing a Burch procedure.

From about 2000 to 2006, I used TVT Retropubic slings and estimate that I performed 600-800 procedures with that device. I then started using the TVT Secur device and continued to use that until 2012 when Ethicon discontinued it. I estimate that I performed approximately 800-1000 procedures to implant TVT Secur. Since the discontinuation of TVT Secur, I have primarily used TVT Abbrevio and TVT Exact to treat SUI. I perform approximately 6-8 TVT Abbrevio procedures per month since 2012 and approximately two per month with TVT Exact. TVT Exact is my sling of choice when a patient has intrinsic sphincter deficiency or has recurrent SUI following a prior sling.

I also have extensive experience in using Ethicon's mesh to treat prolapse, including Gynemesh PS, Prolift, Prolift +M and Prosima. I have been doing vaginal mesh prolapse repairs since approximately 2005. Initially, I began creating mesh "patches" to bolster my traditional vaginal repairs. This work was presented at a national ACOG meeting in 2006 as part of an award winning presentation.

Based on Ethicon's documentation, I received Ethicon-sponsored training to use the following devices: Prolift in December 2005 and June 2009, TVT Secur in September 2006, Prosima and TVTO in March 2010, and TVT Abbrevio in October 2010.

I served as a surgical proctor and preceptor for Ethicon from 2000 into 2011. This teaching primarily occurred at my hospital (Huntington Hospital). On occasion, I would travel to other hospitals to teach or proctor surgeons. I also served as a preceptor for TVT courses for Ethicon including a cadaver course that took place in Baltimore. As with my residents, when

proctoring, I commonly utilized the IFU for educational purposes. I found that the IFU's were the best source of information regarding the device, its insertion, and potential complications. During my time as preceptor, I believed that Ethicon reimbursed me a total of approximately \$50,000.

II. MATERIALS REVIEWED

In the course of preparing this report, I have reviewed the published peer-reviewed medical literature on the Gynecare TVT products, and more generally, the use of midurethral synthetic slings and other surgical procedures to treat SUI. I have reviewed materials produced by Ethicon, including the TVT family of products Instructions for Use (IFU), patient brochures and professional education materials including the TVT Surgeon's Resource Monograph, TVT Secur Key Technical Steps booklet, and procedural videos. I have also read the publicly available materials issued by medical societies and the Food and Drug Administration (FDA) regarding the use of transvaginal mesh to treat SUI. A complete list of the materials that I have reviewed is provided with this Report, and will be supplemented as I review more materials.

III. TYPES OF URINARY INCONTINENCE

Urinary incontinence is the involuntary leakage of urine. There are different types of incontinence, but the two primary types are stress urinary incontinence and urge incontinence.

Stress incontinence is the involuntary loss of urine with increased abdominal stress and/or pressure. Any increase in intra-abdominal pressure – such as that which occurs with coughing, sneezing, laughing or physical activity – increases intra-abdominal pressure and provides a stress on the bladder. That pressure generally does not lead to loss of urine under normal physiologic

conditions. That is because the same pressure applied to the bladder is applied to the urethra. The urethra is a soft pliable tube that is easily compressed against the underlying vaginal wall. As a result, large and sudden increases in intra-abdominal pressure do not generally lead to urine loss because that same pressure is applied to the urethra. In the normal setting, abdominal stress compresses against the urethra against the anterior vaginal wall and a person remains continent.

However, incontinence develops when the vaginal wall weakens. In this situation, the intra-abdominal pressure applied to the urethra does not compress the urethra but instead simply deflects it inferiorly through a weakened vaginal wall. In this situation, abdominal stress puts pressure on the bladder but the pressure on the urethra does not lead to compression of the urethra but instead just deflection of the urethra. This allows the urine to then escape.

An analogy would be stepping on a hose on a hard surface versus a soft surface. If one were to step on a hose on a hard, concrete surface, you could obstruct the flow of water through the hose. However, if that same hose was placed over a bed of sand, the situation would be different. The pressure applied to the hose would simply deflect the hose into the sand but would not compress the hose. As a result, the flow of water through the hose would be unimpeded.

There is a small subset of patients with stress incontinence who suffer from a condition called intrinsic sphincter deficiency. In this group, the sphincter mechanism of the urethra is so weakened that has lost all of its tone. As a result, almost any movement will lead to leakage of urine. In this situation, the vaginal wall (i.e. the backstop) may be strong, but the patient may still experience urine leakage with any type of stress. In my practice, I will typically treat people who suffer from classic stress incontinence (secondary to weakened vaginal wall) with a transobturator sling. Those who suffer from extrinsic sphincter deficiency, I will routinely treat

with a retropubic sling. The retropubic sling is more of a “U-shaped” sling and can be tightened to make up for an intrinsically weak sphincter.

Urgency urinary incontinence is a different process. This is a condition that can be summarized as a “spastic bladder.” In this condition, patients have hyperactive bladder muscles that contract uncontrollably leading to a sensation of urinary urgency and potential incontinence. Urgency urinary incontinence is initially treated with pelvic floor muscle exercises and supportive measures such as voiding diaries, bladder training, and biofeedback. Anticholinergic medication to relax the bladder is also considered first line therapy. Second and third line therapies for an overactive bladder include Botox injections into the bladder to partially paralyze the bladder muscle and prevent uninhibited contractions. Finally, implantable neurostimulators are available that stimulate the sacral nerve roots and reduce bladder tone. These are often considered third line therapy.

Patients who have both stress incontinence and urge incontinence are said to have mixed incontinence. Those patients are often treated with a combination of therapies including surgery and medication.

The American Urological Association’s Guidelines for the Surgical Management of Female Stress Urinary Incontinence (Update 2009) cites a large meta-analysis reporting an estimated prevalence for urinary incontinence of 30% in women aged 30 to 60 years, with approximately half of the cases attributed to SUI, and another study that reported the prevalence of SUI was 5% to 30% in European women. (Updated AUA Guidelines, Appell et al. 2009 (citing Hampel 1997, Hampel 2004)).

IV. IMPACT OF URINARY INCONTINENCE

Urinary incontinence is a devastating condition for the patients who suffer from it. Many patients use a pad to absorb the moisture and control the leakage. However, this can lead to chronic vulvitis and skin breakdown. In addition, constant and continued loss of urine leads to a chronic odor and soiling of one's clothes. Commonly, sheets and bedding are changed on a regular basis to avoid odors related to frequent urine leakage.

This disease has a tremendous emotional impact also. People are forced to curtail their activities. The embarrassment of urinary leakage can lead to a loss of dignity and can severely impact someone's activities of daily living. While urinary leakage is not life threatening, it is extremely embarrassing and distressing to the patient. Perhaps, the negative impact of incontinence is most apparent in the postoperative period when the patient has been cured. As a physician, it is most striking to see the expression of relief and joy expressed by patients. It is perhaps the best indicator as to how this condition can negatively impact one's life.

V. DIAGNOSIS AND TREATMENT OF STRESS URINARY INCONTINENCE

The diagnosis of stress incontinence is based on the patient's history, her physical examination, and an analysis of a urine specimen. According to guidelines from AUGS, urodynamic studies are not required prior to initiating first line treatment for stress incontinence. The work-up requires a urine analysis to rule out underlying urinary pathology, a careful history, and a physical examination. The history should be consistent with stress incontinence and include urine leakage with stress triggers such as coughing, laughing, sneezing and physical

activity. Although the patient may have some symptoms of urgency, in general, her symptoms should not reflect underlying bladder instability.

On physical examination, the diagnosis of urine leakage upon Valsalva maneuver is diagnostic of stress urinary incontinence. According to guidelines from AUGS, if the urine analysis is negative and the history and physical exam are consistent, no further work up is required to initially diagnose or treat this condition.

Urodynamic studies are recommended if the patient has had a previous incontinence procedure, if her symptoms do not suggest pure stress incontinence, or her physical examination suggests another cause of urinary leakage. Urodynamic studies are designed to help provide an objective basis for the patient's symptoms. The goal of urodynamic studies is to evaluate bladder function and to recreate the conditions that lead to urinary leakage. Essentially, the evaluation is designed to differentiate between stress incontinence, urgency incontinence or mixed incontinence. A post-void residual is obtained after the patient empties her bladder. The bladder is then catheterized and filled with fluid. The first sensation of urine is measured, and the capacity of the bladder is also measured. Any uninhibited contractions of the bladder are measured by the bladder catheter. The patient is asked to cough and the bladder is evaluated under this condition of stress. Urine leakage in the presence of a cough confirms the presence of stress incontinence. Uninhibited bladder contractions that lead to urine loss confirm the diagnosis of urgency incontinence. If the both findings are present, then the diagnosis of mixed incontinence is made. Finally, the patient is asked to empty her bladder. Objective measurements are then made of this phase of bladder function. This portion of the evaluation

has little to do with the diagnosis of stress incontinence or urge incontinence. It does rule out, however, underlying bladder dysfunction which may complicate her therapy.

First line treatments for stress incontinence include supportive care measures and pelvic floor muscle exercises. These exercises are commonly referred to as Kegel's exercises. Patients are taught to identify and contract muscles that impede urine flow. They then squeeze these muscles when coughing, laughing or sneezing to help minimize urine loss. Biofeedback and electrical stimulation can be used to augment the teaching and performance of Kegel's exercises. Objective improvements are seen in approximately 30% of patients with this therapy. Other measures to help improve incontinence include timed voiding, minimizing fluid intake, and adjusting medications that may exacerbate urine loss. First line therapy for stress incontinence also includes placement of a suburethral sling. Ultimately, the success rate with surgery and the durability of surgical correction is far greater than any improvement achieved with non-surgical options.

Stress incontinence can also be managed by collagen injections into the urethra. This can be first line or second line therapy. Compared to suburethral slings, collagen injections are uncomfortable, less effective, and need to be repeated every several months to maintain any type of effectiveness. Most patients do not prefer this type of surgery compared to the other options that are available. Occasionally, in the presence of other abdominal surgery, stress incontinence may be treated with a Burch procedure. However, in today's world, this is rather uncommon, if not rare.

VI. THE DEVELOPMENT OF THE MID-URETHRAL SYNTHETIC SLING: TVT RETROPUBIC

Against the backdrop of the various surgical options discussed above, the Gynecare TVT Tension-Free Support for Incontinence (TVT or TVT Retropubic) is a midurethral sling developed by Professor Ulf Ulmsten, with his colleague Papa Petros, ushering in a completely new surgical and conceptual approach to the treatment of SUI. Compared to the Burch procedure or the MMK, the midurethral sling is much less invasive. Compared to the other minimally invasive procedures, the effect is much more durable and long lasting. It is rare to see stress incontinence treated with surgical procedures other than a midurethral sling in today's world.

In the twenty years since its introduction (in Europe in 1997 and in the United States in 1998), the mid-urethral sling, and in particular the TVT sling, has earned a reputation as the "gold standard" of treatment of SUI and is supported by thousands of published clinical studies, including over 100 randomized controlled trials. (April 5, 2013 Email of Medical Director Piet Hinoul and attached study spreadsheets, ETH.MESH.08307644-45). This has been echoed by numerous medical societies comprised of prominent and experienced surgeons in the field of female pelvic medicine, who have issued position statements over the past several years supporting the use of midurethral synthetic slings as a primary treatment option for SUI.

The TVT sling was the outcome of many years of research by Ulmsten and Petros over the 1980s and early 1990s, during which evolved Ulmsten's "Integral Theory." (Petros P & Ulmsten U, 1990). By the early 1990s, this research had developed into a vaginal surgical procedure which involved the placement of a synthetic mesh under the mid-urethra through

small vaginal incisions. (Ulmsten U. et al., Scand. J. Urol. Nephrol. 1995) This was a major departure from existing surgical approaches which involved invasive open abdominal incisions, and an elevation and suspension of the neck of the bladder to surrounding structures, which often resulted in urinary retention and other voiding problems. In addition, the procedure could be performed under local anesthesia with a reduced hospital stay for the patient. For several years, Prof. Ulmsten studied different implant materials such as Goretex, Mersilene and in an attempt to find the most suitable implant material. (Ulmsten U., Int'l. Urogyn. J. 1996). By the mid-1990s, he had selected Ethicon's Prolene mesh as his mesh of choice because it exhibited the least evidence of rejection. (Id.)

In 1996, Ulmsten published the two-year follow up results on his prospective study of this sling on a cohort of 75 patients, reporting that 84% of the patients were completely cured of leakage and 8% significantly improved. In particular, Ulmsten reported that no patient experienced rejection of the mesh and also the a significant increase in quality of life was noted in all patients who were cured or significantly improved. (Ulmsten U., Int'l. Urogyn. J. 1996). The published three year follow up was consistent with this, with 86% of the patients available for follow up (43/50) completely cured and an additional 12% (6 patients) significantly improved. (Ulmsten U et al., Brit. J. Obstet. Gyn. 1999).

Following Ulmsten's initial success with the device, he participated in a prospective trial of six different centers throughout Scandinavia studying 131 patients implanted with the device. This study included investigators and early TVT users Prof. Carl Gustaf Nilsson of Helsinki Finland, and Prof. Christian Falconer of Stockholm, Sweden as well as others. In 1998, the investigators published their 1year results, reporting 91% of the patients cured and 7% significantly improved. (Ulmsten U. et al., Int'l Urogyn. J. 1998). Most patients were released

from the hospital within 24 hours and without a catheter. There were no reports of tape rejection or defective healing. Two uncomplicated hematomas and one uncomplicated bladder perforation were reported. (Id.)

Following the Scandinavian Multicenter trial, Professors Ulmsten, Nilsson and Falconer reported results consistent with the prior trials with a cohort of 90 patients from three centers in Uppsala and Stockholm, Sweden and Helsinki, Finland. Nilsson continued to publish the results after Prof. Ulmsten passed away in 2004. Their results on patients available for follow up were reported at 5 years, 7 years, 11 years and 17 years, representing an extraordinary long term follow up of these patients. At five years, Nilsson reported that of the 72/85 patients appearing for follow up, 84.75 were completely cured and 9% completely improved. No patient complained of long time voiding difficulties, defective healing or tape rejection. Fourteen out of twenty five patients reported relief of their urge symptoms. (Nilsson CG et al., Int'l Urogyn. J. 2001). At seven years, 81.3% of the 80 women reporting for follow up were objectively and subjectively cured, with 6.3% of women reporting de novo urge symptoms and 7.5% reporting recurrent urinary tract infections. (Nilsson CG et al., Obstet. & Gyn. 2004). At eleven years, 90% of the women available for follow up were objectively cured and 77% subjectively cured with 20% experiencing improvement. No late onset adverse events were reported and no tape erosion. (Nilsson CG et al., Int'l Urogyn J. 2008). Finally at seventeen years follow up, 90% of the women available at follow up were objectively cured and 87% subjectively cured or significantly improved. There were no tape complications except for one reported asymptomatic tape extrusion reported by a patient who had not appeared for her eleven-year follow up. Notably, the investigators observed no shrinkage of the TVT over time based on the post void residuals within normal ranges (except for two patients with concomitant diseases). (Nilsson CG

et al, Int'l. Urogyn. J. 2013). My review of the medical literature has not revealed a similar length follow up for any other surgical treatment option for SUI.

VII. MEDICAL LITERATURE SUPPORTING THE USE OF MID-URETHRAL SLINGS INCLUDING TVT

In evaluating the medical literature evaluating the performance of the TVT line of products, I have utilized the Oxford Pyramid of Evidence, picture below, to assess the weight of the evidence and data that is described. Specifically, meta-analyses and systematic reviews of studies, and randomized controlled trials, and deemed among the most reliable and credible forms of studies because of the volume of patient they assess and/or the quality of their methodology. These are followed by prospective or retrospective cohort studies which in general can provide very good information on a device's safety and effectiveness. Towards the bottom of the pyramid are case reports and case series which typically focus on particular complications or notable results that the investigator has observed in a relatively small number of patients. While these reports can be informative and play a role in informing surgeons about infrequently occurring events, they do not provide evidence with the level of reliability as the higher levels of studies, for one reason because they typically do not assess the complications against a denominator of patients who have received the device. This pyramid provides an important general framework within which to assess published data, but of course, specific studies need to be assessed individually for the quality of their methodology and reliability of their conclusions.



Not appearing at all on this pyramid are internal company emails and other product development documentation, on which many of the plaintiffs' experts rely so heavily. While internal company information and testing is informative, particularly as to the historical development of the device, the best assessment of the safety and effectiveness of midurethral slings like TVT are the published studies assessing the *actual performance* of these products in women who are followed over a period of time. That is why the clinical studies are such an important basis of my opinions.

Since the initial studies on TVT Retropubic that were published by Ulmsten and his colleagues over twenty years ago, surgeons throughout the world have conducted studies on TVT Retropubic and its later iterations and have published their findings in publicly-available medical

journals throughout the world. The most reputable of those journals, including many of those cited in this report and on my materials list, employ a rigorous peer review process to ensure the high quality and accuracy of the study's methodology, data analysis and reporting. In a joint position statement issued by the American Urogynecological Society (AUGS) and the Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU), which was originally issued in January 2014 and updated in June 2016, these organizations concluded the following regarding midurethral polypropylene slings including TVT:

The monofilament polypropylene mesh MUS is the most extensively studied anti- incontinence procedure in history. A broad evidence base including high quality scientific papers in medical journals in the US and the world supports the use of the MUS as a treatment for SUI. There are greater than 2,000 publications in the scientific literature describing the MUS in the treatment of SUI. These studies include the highest level of scientific evidence in the peer reviewed scientific literature. The MUS has been studied in virtually all types of patients, with and without comorbidities, and all types of SUI. Multiple randomized, controlled trials comparing types of MUS procedures, as well as comparing the MUS to other established non-mesh SUI procedures, have consistently demonstrated its clinical effectiveness and patient satisfaction. Among historical SUI procedures, the MUS has been studied as long in follow-up after implantation as any other procedure and has demonstrated superior safety and efficacy. No other surgical treatment for SUI before or since has been subject to such extensive investigation.

(Position Statement: Mesh Midurethral Slings for Stress Urinary Incontinence, AUGS/SUFU, issued Jan. 2014, June 2016 (footnotes omitted)). In particular, there are *over 100 randomized controlled trials* that have studied TVT Retropubic. (April 5, 2013 Email of Medical Director Piet Hinoul and attached study spreadsheets, ETH.MESH.08307644-45).

At this time, several studies of TVT with *over ten year follow up* have been published by surgeons throughout the world with results generally consistent with those of the original Scandinavian investigators. Some examples are bulletpointed below:

- Svenningsen et al., Int'l Urogyn. J. (2013): Ten-year follow up on 483 women implanted with TVT. The authors reported an objective cure rate of 90% and subjective cure rate of 76%. 83% considered themselves very satisfied and only 2.3% had undergone further incontinence surgery. De novo urgency was reported by 15% of the patients.
- Serati M. et al., Eur. Urol. (2012): Ten year follow up on 58 women implanted with TVT. No patient required sling release during the follow up period. No patients had significant vaginal, bladder, or urethral erosion. No patients developed de novo dyspareunia.
- Heinonen P. et al., Int'l. J. Urol. (2012): 10.5-year follow up on 138 women implanted with TVT. One patient (0.8%) had a tape erosion into the bladder. Two patients required sling lysis: one patient due to retention at 1 year post-operatively, and another due to pain at 8 years. Both patients' symptoms resolved after sling incision and both maintained continence.
- Aigmueller T. et al., Am. J. Obstet. & Gyn. (2011): Ten year follow up on 201 patients implanted with TVT. 84% had objective clinical cure with a negative clinical stress test. Subjective cure rate was 57%. 23% considered themselves improved. *De novo* urgency was experienced by 20% of the patients.
- Song PH et al, J. Urol. (2014): Thirteen year (mean 162 months) follow up on 206 patients implanted with TVT, presented at the 2014 AUA meeting. The overall cure rate was 83% and satisfaction rate was 68%. At 13-year follow up, one patient was found to have mesh exposure and two patients had *de novo* urgency.

Numerous systematic reviews and meta-analyses have been performed of randomized controlled trials and other studies evaluating TVT products and other brands of mid urethral slings. Novara G. et al. conducted a meta-analysis of 33 RCTs, comparing complications rates of mid-urethral slings to other surgical options for the treatment of SUI. Table 6 of the article lists over 30 studies specific to the TVT device that had 2 years follow-up at the time of the study. Vaginal exposures, where reported at all, ranged from 0.4% to 3.8% with most reported between 1 and 2%. The reported reoperation rates ranged between 1.2% and 3.8%. Voiding dysfunction and UTIs were generally reported at higher rates. (Novara G. et al., Eur. Urol. 2008).

Dmochowski et al. reported the results of the meta-analyses that were the basis for the AUA's 2009 update to its Guideline on the Surgical Management of Female Stress Incontinence. (Dmochowski R. et al., J. Urol. 2010). The analysis considered 436 articles and an additional 155 articles for complications data only. The tables in the article highlight the fact that most of the potential risks of post-surgical urinary complaints are common to all surgeries to treat SUI whether they involve an implant or not. The Panel noted, while acknowledge the risks erosion and extrusion that comes with mesh mid-urethral slings: "Newer techniques and materials for the surgical treatment of stress incontinence have or are being developed. For the index patient, the Panel believes that these techniques, materials, and accompanying physician expertise and experience offer a number of advantages that include shorter operative time, shorter recovery time and less short-term morbidity."

Schimpf et al., on behalf of the Systematic Review Group of the Society of Gynecologic Surgeons, reported on a systematic review and meta-analysis of studies involving thousands of patients undergoing various types of SUI procedures including mid-urethral slings. (Schimpf MO, Am. J. Obstet. Gyn. (2014)). Table 3 to this meta-analysis provides very informative comparisons of complication rates across different procedures to treat SUI, including retropubic, obturator and minislings as well as Burch and fascial slings. While the meta-analysis of subjective cure rates favored midurethral over pubovaginal slings, no significant difference in objective cure rates was found between midurethral slings and Burch colposuspension.

Ford et al. in 2015 published in an updated Cochrane Review an analysis of 81 trials that evaluated 12,113 women. (Ford AA et al., Cochrane Database of Systematic Reviews 2015). Subjective cure rates between transobturator tapes passed using a medial-to-lateral (TVT-O) as opposed to a lateral-to-medial (Monarch) approach were similar (RR 1.00, 95% CI 0.96 to 1.06;

6 trials, 759 women; moderate quality evidence, and RR 1.06, 95%CI 0.91 to 1.23; 2 trials, 235 women; moderate quality evidence).

The 81 trials, which included 12,113 patients through June 2014, demonstrated that “over 80% of women with stress urinary incontinence are cured, or have significant improvement in their symptoms, with either operation [retropubic or obturator sling], for up to five years after surgery.... [T]he information that is available for quality of life shows that it improves as a result of these operations, though there is no clear difference between the two procedures.” The authors also concluded that “mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile.”

VIII. TVT OBTURATOR

After the TVT Retropubic sling had been available for several years, Professor Delorme and others introduced a new way of delivering the polypropylene sling: through the obturator region of the pelvis, rather than behind the pubic bone as with the retropubic approach. Delorme developed the “outside-in” version of the obturator sling. (Delorme E. et al., *Prog. Urol.* 2003). The perceived advantage of the obturator approach to placing the sling was that it would greatly reduce the risk of perforating the bladder, which is more common with retropubic approaches. Rates of bladder perforation in retropubic approaches is estimated in the Schimpf meta-analysis to be 3.6% (as measured in 41 studies covering 11,390 patients, as compared with 0.7% in the obturator approach (as measured in 32 studies covering 4000 patients). (Schimpf MO et al., *Am. J. Obstet. & Gyn.* 2014, Table 3). That said, it is my experience and widely understood within the medical community that bladder perforations that are recognized intraoperatively via

cystoscopy (and most are recognized intraoperatively where a cystoscopy is performed) do not typically result in complications to the patient.

Profession Jean de Leval of the University of Liege, Belgium subsequently developed the “inside-out” version of the obturator technique, which Ethicon ultimately introduced to the market as TVT Obturator or TVT-O. TVT-O featured the same Prolene mesh implant as TVT Retropubic and same midurethral placement, but featured a winged guide and helical passers that delivered the mesh through the obturator foramen medially to the pubic bone, and out the upper thigh/groin area.

Prof. de Leval and his colleague David Waltregny published the results of their initial feasibility study on 107 patients, as well as one- and three-year follow up on a prospective study of 102 patients. (de Leval et al., Eur. Urol. 2003; Waltregny D. et al. J. Urol. 2006). At 1 year, 91% of the patients reporting for follow up (99/102) reported complete cure. No patients had vaginal exposure. Four patients required release for voiding difficulties. Seven percent reported de novo voiding problems. At three years, no erosion or persistent pain was reported; cure was reported in 88.4% and improvement in 9.3%.

TVT-O was launched in early 2004 and has now been on the market for 13 years. In that time, a wealth of peer reviewed medical literature has been published demonstrating that it is equivalent to TVT Retropubic in safety and effectiveness, with a somewhat different complications profile due to the obturator course that it travels. As of 2012, Ethicon had documented over 60 randomized controlled trials that had studied TVT Obturator (several of which also studied other TVT approaches). (April 5, 2013 Email of Medical Director Piet Hinoul and attached study spreadsheets, ETH.MESH.08307644-45).

In fact, several high quality randomized controlled trials studied TVT Obturator against TVT Retropubic or outside-in approaches with *five year follow up or more*:

- Liapis et al., *Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up*, Eur. J. Obs. & Gyn. 148 (2010) 199-201. (115 patients)
- Angioli et al., *Tension-free Vaginal Tape versus Transobturator Suburethral Tape: Five-year Follow-up Results of a Prospective, Randomised trial*, Eur. Urol. 58 (2010) 671-677. (37 TVT-O patients)
- Groutz et al., *Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure*, J. Women's Health, Vol. 20, No. 10 (2011) (61 patients)
- Cheng, et al., *Tension-free vaginal tape-obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow up*, Eur. J. Obstet. & Gyn., 161 (2012) 228-231 (100 patients)
- Serati et al., *TVT-O for the Treatment of Pure Urodynamic Stress Incontinence: Efficacy, Adverse Effects and Prognostic Factors at 5-Year Follow up*, Eur. Urol. 63 (2013) 872-878 (185 patients)
- Laurikainen et al., *Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence*, Eur. Urol. 65 (2014) 1109-1114 (123 TVT-O patients). In particular, the authors here found that "No late onset adverse effects of the used tape material were seen."
- Athanasiou et al., *Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail?* Int. Urogyn. J. (2014) 25:219-225 (124 patients)
- Zhang et al., *Retropubic tension-free vaginal tape and inside out transobturator tape: a long term randomized trial*, Int. Urogyn. J. (July 2015) (62 TVTO patients).
- Tommaselli et al., *Tension-free vaginal tape-obturator and tension-free vaginal tape-Secur for the treatment of stress urinary incontinence: a 5 year follow up randomized study*, Eur. J. Obstet. & Gyn. 185 (2015) 151-155 (58 TVT-O patients).
- Cheung et al., *Inside out versus outside-in transobturator tension-free vaginal tape: A 5-year prospective comparative study*, Int'l J. Urol., (2014) 21, 74-80 (82 TVT-O patients).

While these studies report different ranges of individual complications, they are relatively uniform in reporting similar effectiveness for the two approaches.

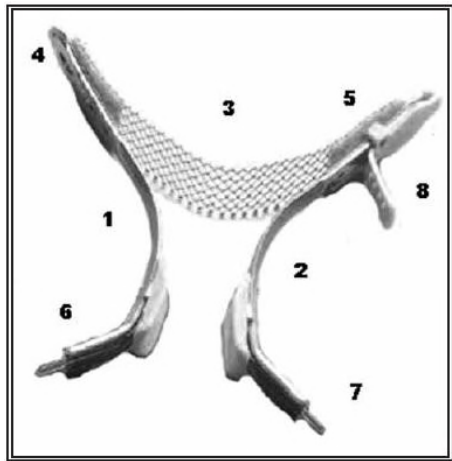
Ford AA, et al., the authors of the 2015 Cochrane Review on slings, concluded that: “Irrespective of the routes traversed, [midurethral slings] are highly effective in the short and medium term and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI. With the exception of groin pain, fewer adverse events occur with employment of a transobturator approach. When comparing transobturator techniques of a medial-to-lateral versus a lateral-to-medial insertion, there is no evidence to support the use of one approach over the other.”

In addressing the potential risks of midurethral slings, the authors stated that “tapes passing behind the pubic bone (retropubic) seem to carry a greater risk of injuring the bladder during the operation and of women experiencing problems emptying their bladder completely after surgery. However, this operation leads to less groin pain in the short term. There is some limited evidence that this way of inserting the tape has a lower risk of requiring a repeat operation in the long term compared to tapes passing through the groin (transobturator). There is moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved.” (Ford AA, et al., 2015, at 30.) Ultimately the authors found that “women’s outcome for quality of life and sexual function improved significantly after all surgical approaches” of mid urethral sling. (*Id.* at 47.)

IX. TVT SECUR

In 2006, Ethicon introduced its next iteration on the TVT sling, TVT Secur. TVT Secur is a single incision sling that has the advantage of avoiding retropubic or transobturator exit sites.

As a result, it was less invasive and associated with less discomfort than the other types of mid urethral slings. It could be placed in a retropubic position or a transobtruator position.



TVT Secur was innovative because it was a single incision sling. As a result, the postoperative discomfort was minimal at worst. Full length transobtruator slings require exit wounds through the obturator foramen and through the adductor muscles of the thigh. Once placed, the mesh remains in the adductor muscle compartment. This can lead to discomfort in the inner thigh for a few days. In rare cases, obturator nerve impingement can occur which leads to more prolonged discomfort and dysfunction. As discussed later in this report, full length retropubic slings are associated with a risk of bladder injury. Furthermore, the retropubic slings require exit wounds in the suprapubic region, which can cause lower pelvic discomfort. In addition, these slings are associated with a small risk of retropubic hematoma. The TVT Secur did not require these exit wounds. The sub-urethral area is an area with minimal pain fibers. The vaginal epithelium in that region is associated with few pain fibers. As a result, placement of this sling resulted in minimal or no postoperative discomfort to the patient.

After TVT Secur was introduced, it quickly became my primary mid-urethral sling of choice. I placed the sling under a “saddle-block” anesthetic. This is essentially a low spinal anesthetic. As a result, I was able to tension these slings in a very dynamic setting. The patient was able to cough with a full bladder, and the sling was tightened until her incontinence was cured. This helped minimize the risk of over or under tightening of the sling and resulting in very high incontinence cure rates postoperatively.

While the initial benefits of the TVT Secur sling, particularly in terms of patient discomfort, were immediately apparent, I was somewhat apprehensive about the long term success. However, it also became very clear that the durability of this sling seemed to match the durability of full length slings. I found very few clinical failures in my practice, despite using the TVT Secur as my primary urethral sling. Subsequent peer review data confirmed my clinical impression.

Because of my positive experience with TVT Secur, I was very disappointed when Ethicon discontinued it in 2012. At that time, I started the TVT Abbrevio sling which is now my sling of choice for most cases. This is a modified transobtruator sling. Because it involves a transobtruator approach, there is minimal risk of bladder injury. The Abbrevio is 12 cm in length, and there is minimal mesh contact with the adductor muscles of the thigh. As a result, there is less postoperative discomfort than with traditional full-length transobtruator slings. However, this sling does require the typical exit wounds in the region of the inner thigh.

In the several years that TVT Secur was on the market, several published studies that reported results indicating that, in general, TVT Secur demonstrated equivalent or slightly less effectiveness than full length slings, but with less post-operative pain.

In 2007, the first year after TVT Secur was launched, the International Urogynecology Journal published the results of several abstracts on TVT Secur that were presented at the 2007 meeting of the International Urogynecological Association (IUGA). The results of the studies are summarized in the chart below.

GYNECARE TVT SECUR[®] System Abstracts IUGA 2007¹						
Author(s)	# Pts	Mean f/u	Subjective Cure	Failed/ Worse	Objective Cure	Complications/ Comments
Albrich et al, Germany	18 (H-U n/a)	18 wk	77.7%	16.7%	-cst 83.3% +cst 16.7%	4 exp all mg with E ₂
Marsh et al, UK	40 (H-U n/a)	6 wk	74% dry 12% imp	14% no Δ		1 "buttonhole" 2 vd Dyston 1 exp/1 pain
Shaare-Zedek, Israel	150	n/a	97%	3% no Δ		5 unintended device removal
Morton et al, Czech Rep	25 (15-H/10-U)	1-5 mo	88%	12% no Δ		
Saltz et al, USA	77 (27-U/50-H)	6 wk	68.8% dry 13% imp	3% worse		2.6% vd Dyston 1 pain
Karram et al, USA	60 (29-U/31-H)	6 wk	86.7% >50% imp on VAS	3% worse	-cst 75% +cst 25%	1 bladder perf 3 de novo OAB 1 exp
Debodinance et al, France	40 (all H)	8 wk	76.9% dry 15.4 imp	7.7% no Δ		5 vd Dyston 1 exp De novo OAB/UII-20%
Totals (not a meta analysis)	410	6.6 wk	85.4%	8.5% no Δ 6% worse	-cst 77% +cst 23%	

1. *Int Urogynecol J.* :18 (Suppl): S1-S24, S25-S105, S107-244; 2007.

Of these early studies, that by Neuman and Shaare-Zedek involved the largest cohort, 150 patients. With respect to complications, the authors reported no voiding difficulty, no

significant pain, and no other patient inconvenience was observed post-operatively. The early therapeutic failure rate was only 3% (although this was lower than several other of the studies referenced). No bowel, bladder or urethral injuries were reported. No intraoperative bleeding or post operative infections were present. Five patients had unintended tape removal at the time of insertion.

In the ensuing years, TVT Secur continued to demonstrate consistent effectiveness rates in studies with one year follow up. Meschia et al. reported a 78% success rate in a multi-center prospective trial at one year follow up on 91 patients. (Meschia M. et al., Int'l. Urogyn. J. 2009). Oliveira et al. reported 85% cure and improvement in 106 patients at a mean 15 month follow up. (Oliveira R. et al., BJU Int'l. 2009). Pardo et al. reported 91.7% of patients cured at 12 months follow up with an additional 5% partially cured or improved. (Pardo J. et al., Int'l. Urogyn. J. 2010). Dmochowski et al. reported an objective cure rate of 87.5% among the 642 TVT Secur patients in the TVT World Registry, as well as an improvement in the quality of life that did not seem to deteriorate over one year. (Dmochowski et al., J. Urol. 2009).

TVT Secur has also been studied in meta-analyses as well as numerous randomized controlled and other comparative trials. Walsh et al. published a meta-analysis of multiple studies with one-year follow up conducted between 2006 and 2009, reporting mean objective and subjective cure rate of 76% at 12 months, exposure rate of 2.4% , dyspareunia rate of 1% and return to the OR for post operative complications was 0.8%. (Walsh CA et al., BJUI 2011).

Lee HN et al. reported 3 year follow up on an RCT comparing TVT Secur patients implanted with the "U" retropubic approach v. the "H" or "hammock" obturator approach. 115 patients were included in the study and 102 were available for three year follow up. The overall

cure rate at the 1, 2 and 3 year follow ups were 87.8%, 83% and 79.4% respectively. There were no difference in cure rates between the U and H approaches. 83% of patients were satisfied with the surgical outcome at the 1- and 3-year follow-ups. Quality of life and symptoms (I-QoL, BFLUTS-SF, and I-VAS) were improved from baseline regardless of the approach used at the 1- and 2-year follow-ups. The authors concluded that both the “U- and H-type approaches of TVT-Secur for the treatment of female SUI remains efficacious, safe, and satisfactory for up to 3 years after surgery. (Lee HN. et al., Low Urin. Tract Symptoms 2015).

Biancho-Ferraro et al. reported two-year outcomes on an RCT comparing TVT Secur to TVT Obturator. At two years, objective cure rates were 77.3% in the TVT Secur group and 83.6% in the TVTO group. Subjective cure rates were 75.7% in the TVT Secur group and 80.3% in the TVTO group. Tape exposure was observed in both groups and groin pain in the TVTO group. The authors concluded that the efficacy of TVT Secur was similar to that of TVTO at two years. (Biancho-Ferraro AM, Int’l. Urogyn. J. 2014).

Hinoul et al. reported one year follow up on an RCT in which 75 patients received TVT Secur and 85 received TVT Obturator. SUI was reported by 24% of the Secur patients and 8% of the Obturator patients. SUI could be objectified in 16% of the Secur patients and 2% of the Obturator patients. The authors found that Secur patients experienced significantly less pain in the first two weeks after surgery than the TVTO patients. (Hinoul P. et al. J. Urol. 2011).

Tommaselli et al. published 5-year follow up on an RCT where 154 patients were allocated to TVTO and TVT Secur. 120 patients were evaluated only subjectively and 84 both objectively and subjectively. At five years, subjective success was 79% for TVTO and 63.8% for TVT Secur. Objective success was for 82.6% for TVTO and 68.4% for TVT Secur. Rates of

post operative urinary symptoms were similar between the two groups. The authors concluded that TVT Secur was not inferior to TVTO in subjective success but showed a trend toward lower efficacy. (Tommaselli G., Eur. J. Obstet. Gynecol. Reprod. Biol. 2015).

Tang et al. reported 2 year follow up on a RCT of TVT Secur v. TVT Obturator, finding no significant difference in cure and improvement rates at 6, 12 and 24 months. Subjective satisfaction was greater than 90%. Operative time was significantly shorter in the TVT Secur group and groin pain was higher in the TVT Obturator group. Quality of life significantly improved in both groups. There was a significant difference in the PISQ scores postoperatively in the TVT Secur group. Only 1 out of 39 patients in the TVT Secur group reported dyspareunia (2.6%). (Tang X et al., Menopause 2014).

Abdelwahab et al. randomly assigned 30 patients to TVT Retropubic and 30 to TVT Secur. The authors reported that, at 9 months follow up, 90.1% were cured in the TVT Retropubic group and 93.4% in the TVT Secur group. Operative time and intra-operative morbidity were significantly lower in the TVT Secur group. The authors concluded that TVT Secur is “could be considered as a safe, easy and effective alternative to TVT with less morbidity.”

Table 3 of the Schimpf meta-analysis nicely summarizes complication rates reported over 15 randomized controlled trials of mini-slings. Fourteen of the 15 trials involved TVT Secur, indicating that it is by far the most studied mini-sling. Those complication rates are summarized in the following chart:

<i>Complication</i>	<i>Table 3 – Rates of Adverse Events with TVT Secur and Minislings</i>
Estimated blood loss > 200 mL	1.1%
Transfusion	0.51%
Hematoma	0.85%
Return to operating room for erosion	1.4%
Exposure	2.0%
Wound infection	0.31%
Urinary tract infection	3.6%
Bowel injury	0.74%
Nerve injury	0.00%
OAB / Urgency	5.4%
Retention lasting < 6 weeks post-op	2.1%
Retention lasting > 6 weeks post-op	3.3%
Return to O.R. for urinary retention	1.9%
Groin pain	0.62%
Leg pain	1.6%
Bladder perforation	0.85%
Urethral perforation	2.70%
Vaginal perforation	1.3%

X. PUBLIC STATEMENTS BY MEDICAL SOCIETIES AND THE FDA ON THE USE OF SYNTHETIC MIDURETHRAL SLINGS.

As referenced above, over the past several years, several medical societies representing urologists, gynecologists and urogynecologists throughout the world have recognized the midurethral sling to be the gold standard treatment for SUI and a great advancement in women's health. Those discussed below are just a few examples of a larger body of public statements.

In November 2011 the American Urological Association (AUA) released a Position Statement on the use of vaginal mesh for the treatment of SUI. Based on Level 1 evidence and a 10 year follow up, the AUA concluded the efficacy of synthetic polypropylene mesh slings are equivalent or superior to other surgical techniques and are not associated with a significant increase in adverse events. The statement concludes "synthetic slings are an appropriate

treatment choice of women with stress incontinence, with similar efficacy but less morbidity than conventional nonmesh techniques.” This statement followed the AUA’s issuance in 2009 of an updated Guideline for the Surgical Management of Female Stress Urinary Incontinence, in which the AUA performed a meta-analysis of studies of synthetic midurethral slings, citing 81-84% cure rates. The AUA further noted that the synthetic midurethral sling had “largely replaced the retropubic suspension and the autologous sling as the primary procedure for SUI.”

The joint position statement of AUGS and SUFU, issued in January 2014 and updated in June 2016 concludes:

The polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy it has created an environment for a much larger number of women to have access to treatment. In the past, concerns over failure and invasiveness of surgery caused a substantial percent of incontinent women to live without treatment. . . . This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.

In July 2014, the International Urogynecological Association (IUGA) added its own voice to the growing number of statements issued by the medical societies who supported the use of synthetic midurethral slings in women:

“There is robust evidence to support the use of MUS from over 2,000 publications making this treatment the most extensively reviewed and evaluated procedure for female stress urinary incontinence now in use. These scientific publications studied all types of patients, including those with co-morbidities such as prolapse, obesity, and other types of bladder dysfunction. It is, however, acknowledged that any operation can cause complications. For MUS, these include bleeding, damage to the bladder and bowel, voiding difficulty, tape exposure and pelvic pain; all of these may require repeat surgery but this is uncommon. Nevertheless, the results of a recent large multi-centre trial have confirmed excellent outcomes and a low rate of complications to be expected after treatment with MUS. Additionally, long term effectiveness of up to 80% has been demonstrated in studies including one which has followed up a small group of patients for 17 years.”

Most recently, in November 2015, a Joint Practice Bulletin issued jointly by ACOG and AUGS regarding Urinary Incontinence in Women, making the following conclusions and recommendations are “based on good and consistent scientific evidence (Level A)....”:

- Synthetic midurethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension. Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic midurethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic midurethral slings.
- There are substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress urinary incontinence in women.

While the medical societies were assessing the safety and effectiveness of midurethral slings, the U.S. Food and Drug Administration (FDA) was doing its own assessment. On October 20, 2008, the FDA issued a public notification informing surgeons that it had received over 1000 complaints alleging complications following the use of surgical mesh to treat either prolapse or SUI. The FDA did not specify how many complaints were specific to SUI treatment and did not identify any particular brand of sling. Over the next few years, the FDA conducted a review of complaints submitted to the agency and a systematic review of medical literature assessing prolapse and SUI meshes.

In July 2011, it issued an updated public notification that was specific to transvaginal mesh to treat prolapse but specifically excluded an analysis of slings to treat SUI. The FDA also issued a lengthy Executive Summary in which it concluded as follows after its review of the literature on slings:

Overall, although there is a variety of minimally invasive synthetic slings that are placed differently, these slings appear to be as effective as open retropubic colposuspension. Outcomes data are predominantly relatively short term (1-2 years), however. The bottom-to-top retropubic approach appeared to be more effective in the short term compared to top-to-bottom retropubic approach. Monofilament tape appeared more effective than multifilament tapes. Objective and subjective cure rates

were high for both transobturator and retropubic slings, with a slight advantage going to the retropubic approach.

(FDA Executive Summary, July 2011). In September 2011, the FDA convened an Advisory Panel to hold two days of hearings on the evidence surrounding the use of mesh transvaginally to treat prolapse and SUI.

Two years later in March 2013, the FDA issued a public statement entitled Considerations About Surgical Mesh for SUI, based on the results of its literature and complaint review and hearings, in which the FDA arrived at the following conclusions:

- The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year. Longer follow-up data is available in the literature, but there are fewer of these long-term studies compared to studies with one-year follow-up.
- The safety and effectiveness of mini-slings for female SUI have not been adequately demonstrated. Presently, it is unclear how mini-slings compare to multi-incision slings with respect to safety and effectiveness for treating SUI. Additional studies may help the agency to better understand the safety and effectiveness of these devices.
- Mesh sling surgeries for SUI have been reported to be successful in approximately 70 to 80 percent of women at one year, based on women's reports and physical exams. Similar effectiveness outcomes are reported following non-mesh SUI surgeries.
- The use of mesh slings in transvaginal SUI repair introduces a risk not present in traditional non-mesh surgery for SUI repair, which is mesh erosion, also known as extrusion.
- Erosion of mesh slings through the vagina is the most commonly reported mesh-specific complication from SUI surgeries with mesh. The average reported rate of mesh erosion at one year following SUI surgery with mesh is approximately 2 percent. Mesh erosion is sometimes treated successfully with vaginal cream or an office procedure where the exposed piece of mesh is cut. In some cases of mesh erosion, it may be necessary to return to the operating room to remove part or all of the mesh.

- The long-term complications of surgical mesh sling repair for SUI that are reported in the literature are consistent with the adverse events reported to the FDA.
- The complications associated with the use of surgical mesh slings currently on the market for SUI repair are not linked to a single brand of mesh.

XI. PROPER PLACEMENT OF THE SLING

A well-known risk of sling surgery is the potential to overtension the sling. The TVT product IFUs instruct surgeons to place the slings in a tension free manner and warn that overtensioning can results in obstructive symptoms.

If a sling is overtensioned, then it may show evidence of curling and will not lie flush against the suburethral tissue. One of the procedural points that I repeatedly stress with my residents is to inspect the positioning of the mesh following mesh placement and removal of the mesh arms. The mesh should lie against the suburethral tissue gently and flat. The term used to describe proper placement of the mesh is “quilting.” Like a stitched quilt, the suburethral tissue should gently bulge through the holes of the mesh and should not be strained. The other technical point that I stress with the residents is to check for “button holing” of the mesh through the anterior fornices. I have not seen evidence of slings curling in the absence of overtensioning.

The TVT IFUs recommend that the surgeon place an instrument between the mesh and the suburethral tissue when removing the mesh sheath. This facilitates placement of the mesh in tension-free manner and prevents over tightening of the sling. Typically, I use a #8 Hagar dilator, but other types of instruments are also commonly used.

XII. MATERIAL PROPERTIES OF PROLENE MESH

Many of plaintiffs' expert witnesses have suggested that the Prolene mesh that comprises the tape in TVT slings is not suitable to treat SUI. In particular they claim that the mesh degrades, is cytotoxic, that its pore size is too small, that the mesh contracts, ropes and curls and that it causes a chronic foreign body reaction that is harmful to patients. I disagree with these arguments and have concluded that Prolene is a safe and effective material for this use.

The use of Prolene as an implant in the human body, both as a mesh and as a suture, goes back decades. Prolene sutures have been utilized for decades in surgery throughout the body, including in cardiac surgery. Prolene meshes have been utilized to repair hernias since the 1970s, now 40 years. And as discussed above, starting with the 1996 publication of patients by Prof. Ulmsten and Nilsson, we now have over 20 years of published literature from surgeons throughout the world tracking their performance of this mesh used in this indication. That data has been published at every level of study but most importantly in RCTs and systematic reviews and metanalyses – the highest levels of evidence. (Oxford Pyramid). The position statement issued jointly by AUGS and SUFU and updated as recently as June 2016 reports that: “There are greater than 2,000 publications in the scientific literature describing the MUS in the treatment of SUI. These studies include the highest level of scientific evidence in the peer reviewed scientific literature.” Several of these studies are discussed in detail above in this report. These claims of dangerous material propensities falter in the face of this avalanche of clinical data.

The Prolene mesh in the TVT slings is macroporous, Type 1 mesh under the Amid classification. Under that classification system, meshes with pore sizes over 75 microns are macroporous. (Amid 1997). The pore size of the mesh in TVT is 1379 microns, far in excess of

that. (Moalli P. et al. Int'l. Urogyn. J. 2008). The position statement of AUGS/SUFU further recognizes the Prolene in TVT as macroporous where it states: "As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years", citing as its reference the 17 year follow up study published by Prof. Nilsson on TVT Retropubic.

There is no credible body of evidence in the published medical literature that demonstrates that Prolene mesh degrades after implantation in any way that manifests clinically for patients. That conclusion is inconsistent with the numerous TVT studies discussed above reporting high success rates even at follow up of ten years or more. Polymer scientists Thames et al. cleaned explanted Prolene and found that "Our effective cleaning of explanted Prolene meshes and subsequent analyses showed that they did not degrade in vivo. Instead, the cracked layer that some researchers have identified as degraded Prolene is an adsorbed protein-formaldehyde coating, resulting from the well-established formalin-protein fixation process that occurs immediately upon placing an explant in formalin." (Thames, SF et al., Int'l Urogyn. J. 2016). In the responses to Frequently Asked Questions published jointly by AUGS and SUFU in 2014, those two organizations specifically pointed to the long history of the use of polypropylene as midurethral slings in rejecting the notion that any 'surface-cracking' on polypropylene has a clinical impact on patients. (AUGS/SUFU Frequently Asked Questions to Providers, Mid-urethral slings for SUI, March 12, 2014). In Woodruff's histopathologic analysis on 24 explants (polypropylene, autologous fascia, porcine dermis, cadaveric dermis and cadaveric fascia) at 2-34 months after implantation, no graft degradation had occurred in the polypropylene material. (Woodruff AJ et al., Urology 2008).

In support of their degradation theories, Plaintiffs' experts often rely upon the study published by Henri Clave et al., which reported on explanted mesh implants from women with mesh erosion and/or 'infection' after mesh augmented reconstructions in comparison to a control group of new mesh implants. However, this single study cannot be the basis for a conclusion that Prolene mesh degrades in the body, not only because of the small study population, but also because the study does not examine meshes implanted in women who are not experiencing complications. Even the study authors acknowledge that the oxidation of polypropylene "can neither be confirmed nor excluded' in the in-vivo environment" and "prediction of normal in-vivo sling material aging or the range of consequences in the clinical state beyond the observed samples is not possible. Due to small effective sample size, it is not possible to categorically conclude on the basis of statistical analysis even if a clear tendency is present." (Clave H. et al., Int. Urogyn. J. 2010).

I have explanted mesh on a number of patients. Most of these patients have been referred to my practice from outside sources. At the time of surgery, I have never seen any evidence of degradation of polypropylene mesh. Usually, the mesh is nicely incorporated into the tissues. I have seen evidence of chronic inflammation associated with mesh erosion and/or extrusion. However, the mesh itself has never shown any evidence of degradation.

Plaintiffs' experts also suggest that the contraction of the mesh tape causes severe and prolonged pain and other complications. Certainly, it is a known and expected phenomenon of wound healing that when the mesh sling is implanted, the tissues that surround the mesh will contract to some extent as the mesh becomes integrated into the tissue. This is precisely why the IFUs for the TVT products and accompanying professional education instruct doctors to implant the mesh loosely and without tension. However the medical literature does not support the

notion that such contraction results in complications and pain for patients where the mesh is properly placed and not overtensioned. To the contrary, in their 17 year following up on their 90 patient cohort, Nilsson et al. reported no shrinkage based on post void residuals. (Nilsson CG et al., Int'l Urogyn. J. 2013). This is consistent with the findings of Lo and Dietz who performed ultrasound analysis of TVT slings and did not find evidence of such shrinkage. (Lo TS et al., J. Urol. 2004; Dietz HP, Am. J. Obstet. & Gyn. 2003). In particular, Lo et al. concluded: "The TVT sling fixes to its original implanted site along the urethra and appears to slowly descend with the surrounding tissue with time."

The argument for shrinkage or contraction of the mesh over time is also contradicted by two consistent clinical observations. Number one, the short term urinary retention that occasionally occurs following placement of mid-urethral slings virtually always resolves with observation and bladder draining. Number two, initial cure rates tend to decline over time. If the mesh were to contract or shrink, neither of these observations would be true. Lo's observation of slow descent is consistent with these clinical observations.

Finally, Plaintiffs' experts portray the chronic foreign body reaction that ensues following the implantation of a TVT sling as a severe adverse event resulting in long-lasting and severe complications. That is not the case. If it were the case, chronic pelvic pain would be reported frequently in the thousands of published studies on midurethral slings, and it is seldom reported. When the mesh is first implanted, this generates an acute inflammatory process that, after a period of time, evolves into the body's normal process of integrating the implant into the body's tissues. This is not an adverse event, it is an expected histological process (as it is with other implanted foreign bodies, such as breast implants). While I am not a histologist or pathologist,

neither my review of the medical literature nor my extensive experience implanting slings and providing post-operative treatment supports the notion that the chronic foreign body reaction generates severe complications for patients.

XIII. COMPLICATIONS

There is a known body of potential risks or adverse events that are common to all forms of surgical treatment of SUI, and midurethral slings are no exception. These include recurrence of incontinence, urinary retention, voiding dysfunction, urinary tract infection, tissue and organ damage, nerve damage, overactive bladder symptoms (include frequency, urgency and urge incontinence), hematoma, wound complications, vaginal pain, pelvic pain and pain with sexual intercourse. These risks of SUI surgery are widely known by surgeons based on their training and based on the fact that they are reported in the published medical literature. Mesh exposure, extrusion and erosion is the only risk of slings that is unique to mesh.

Urinary Retention

Urinary retention is the patient's inability to void. In order to avoid the risk of retention, the IFUs of several TVT products advises surgeons to place a blunt instrument between the urethra and the tape during the removal of the tape sheaths "to avoid positioning the tape with too much tension."

While urinary retention is a risk of any surgery to treat SUI, reliable meta-analyses report higher rates of retention with Burch than with midurethral slings. Schimpf et al. reported retention lasting less than six weeks and more than six weeks at the following rates:

	<u>< 6 weeks</u>	<u>> 6 weeks</u>
Minislings	2.1%	3.3%
Obturator	2.3%	2.4%
Retropubic	3.1%	2.7%
Pubovaginal	12%	7.5%
Burch	17%	7.6%

The AUA Guidelines report median 3-4% retention rates in retropubic suspensions such as Burch as well as midurethral slings, and report 8% in autologous fascial slings. (AUA Guidelines 2009, Table 4).

When urinary retention does occur, it is usually best managed conservatively. Typically, most patients will respond to extended transurethral urinary catheterization. This period of catheterization may last anywhere from three days to two weeks. If prolonged catheterization is required, I will typically teach people to self-cath. This provides them with less discomfort and allows them to resume normal activities. Most patients readily adapt to this approach. There are physicians that teach all of their patients undergoing mid urethral sling operations to self-cath preoperatively. Given the low rates of retention, I think this is a rather unnecessary approach.

Should a patient's urinary retention persist after weeks of catheter drainage or self-cathing, then surgical correction may be indicated. This is usually a simple procedure to perform. A small incision is made in the suburethral area and a simple incision is made in the sling. The vaginal epithelium is closed over the sling. No other attempts are made to alter the sling position intraoperatively. I have found that simple sling incision usually is enough to relieve the patient's retention without significantly increasing the risk for recurrent stress

incontinence. My clinical impression is well supported by the peer review literature in this regard.

Overactive Bladder

Overactive bladder symptoms include frequency, urgency and urge incontinence. De novo urge symptoms, like retention, is a risk of any surgery to treat SUI. The TVT product IFUs provide in the Warnings section that: “As with other incontinence procedures, de novo detrusor instability may occur following a suburethral sling procedure.... To minimize this risk, make sure to place the tape as described above.”

The Schimpf meta-analysis reported the following rates for overactive bladder/urgency among different types of SUI procedures, reflecting relatively consistent rates among the procedures:

Burch	4.3%
Obturator	5.3%
Minisling	5.4%
Retropubic	6.9%
Pubovaginal	8.6%

The AUA Guidelines report that de novo urge incontinence occurred in a median of 8% of patients undergoing Burch, 9% of patients undergoing autologous fascial slings without bone anchors, 28% of patients undergoing cadaveric slings with bone anchors, and 6% of patients undergoing synthetic slings at 12-23 months postoperatively. (AUA Guidelines 2009, Table 3).

While TVT slings are not designed or indicated to treat overactive bladder symptoms, some studies have reported improvement of urge symptoms. (Hijaz A., AUA News 2014; Waltregny D., Eur. Urol. 2007).

Cystitis/Urinary Tract Infection

“Cystitis” refers to an infection of the bladder. Typically, people will refer to these as “UTI’s.” A urine culture is the diagnostic test to prove the absence or presence of cystitis. It is typically successfully treated through a course of antibiotics. The criteria necessary to diagnose this depends on whether the patient is symptomatic or not. AUGS guidelines vary regarding the criteria necessary to diagnose cystitis based on the patient's symptoms and urine culture results. Generally speaking, urinary tract infections are considered “recurrent” if more than two culture proven infections occur over a six month period. There are multiple risk factors for cystitis. These would include but are not limited to age, estrogen status, sexual activity, instrumentation of the bladder, and the existence of other urinary tract pathology such as stones or diverticuli. AUGS is considered the authority on the criteria to diagnose and treat urinary tract infections. They are also the authority that can be used to cite the definition for recurrent bladder infections.

Schimpf reports UTI rates of 5.9% for Burch, 4.2% for pubovaginal slings, 4.3% for obturator, 3.6% for minislings, and 11% for retropubic. (Schimpf, Table 3). The Novara meta-analysis lists numerous studies providing 24 month follow up on patients implanted with TVT Retropubic, providing a range of 1.5% to 15% of patients with UTI. The TOMUS RCT comparing TVT Retropubic to TVT Obturator reported UTI rates of 1% in the retropubic group and 0% in the obturator group. (Brubaker L. et al., Am. J. Obstet. & Gyn. 2011). These rates are

consistent with those reported in the Albo study which compared Burch to fascial sling. (Albo ME, N. Engl. J. Med. 2007).

Bladder perforation and hematomas

A known risk of the retropubic approach is injury to the bladder. The reported rates of bladder injury typically range from less than 5% to approximately 10%. (Novara meta-analysis 2008). Megan Schimpf et al. reported in the 2014 SGS Systematic Review at 3.6% rate of bladder perforation in retropubic slings in 41 studies spanning 11,390 patients. The requirement of cystoscopy with the TVT Retropubic sling (described in the IFU) minimizes incidents of unrecognized bladder perforation. When bladder injury does occur and is recognized, the trocar is simply removed and replaced into its proper position. Long term sequelae such as pain or scarring is incredibly rare. Schimpf reports rates of 2.8% for Burch, 2.3% for pubovaginal slings, 0.7% for obturator, 0.85% for minislings, and 3.6% for retropubic. (Schimpf, Table 3).

Retropubic slings are also associated with retropubic hematomas, although these are quite uncommon. Should a hematoma develop, they usually spontaneously resolve and rarely are associated with chronic pain.

Dyspareunia

While pain with intercourse is a risk of any pelvic surgery, the medical literature does not reflect frequent reporting of dyspareunia after a midurethral sling, particular in the absence of concomitant surgeries. The Ford Cochrane Review of midurethral slings, issued in 2015, found that “problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved.” (Ford AA, et al., 2015, at 30.) The authors found that “women’s outcome for quality of life and sexual function improved significantly after all surgical

approaches” of mid urethral sling. (*Id.* at 47.) The Schimpf meta-analysis reported: “Dyspareunia is rare with any type of sling...”, citing an incidence of less than 1% for all types of slings. (Ford AA, Cochrane Review 2015; Schimpf Table 3).

Zyczynski et al. assessed the effects of midurethral sling surgery on sexual function during the two year follow up on the TOMUS RCT comparing TVT Retropubic to TVT Obturator. They reported the mean sexual function scores improved significantly in both groups with no significant difference between the two. (Zyczynski HM et al., Am. J. Obstet. & Gynecol. 2012).

Pelvic pain

The etiology of pelvic pain following placement of mid urethral slings is often complicated, multi-factorial, and difficult to ascertain. Chronic pelvic pain is not rare. It can be a vexing condition to treat and often has multiple etiologies. Objective disease state such as endometriosis, pelvic adhesive disease, uterine fibroids, adenomyosis and ovarian cysts have also been associated with chronic pain. Urogenital atrophy is a virtually universal condition in postmenopausal women. It is typically associated with chronic pain and dyspareunia. Obstetrical injury and/or lacerations can also lead to vaginal deformities, vaginal scar tissue and chronic pain. There are also psychosocial issues, such as a history of sexual abuse, which can be associated with chronic pain and dyspareunia. Spasms of the pelvic floor muscles can lead to vaginismus and chronic pain. Multiple vulvar conditions including lichen sclerosis and chronic vulvitis can lead to persistent discomfort. All of these conditions are more common than surgically associated discomfort. This list is not meant to be inclusive or complete.

The surgical technique associated with placement of a mid urethral sling usually has little impact on a patient's chronic pain. Where a patient experiences pain with a sling, it is typically in the context of an erosion or related to the healing process and/or formation of scar tissue. Over tensioning can lead to urinary retention, but this should not cause chronic pain. Actual mesh erosion or exposures following mid urethral sling placement is actually a relatively uncommon event. In my experience, the mesh erosion rate is well less than 1%, and the literature typically reports an exposure rate around 2% as discussed below.

Groin pain

Post-operative groin pain is most often seen in transobturator procedures, as the helical passers that deliver the mesh travel through the obturator space. Most patients do experience some mild inner thigh discomfort following placement of transobtruator mesh. This usually is transient in nature and does not indicate the presence of a nerve injury. In most cases, this pain resolves within a few days of the surgery. The TVT-O IFU correctly warns that “transient leg pain lasting 24-48 hours may occur and usually be managed with mild analgesics.” Schimpf reported groin pain rates of 6.5% in obturator slings, 1.5% in retropubic slings, 1.1% in Burch procedures, and less than 1% in minislings and Burch procedures. (Schimpf Table 3). Persistent or severe complications associated with the transobturator passage are reported, but are rare. (Walters M. et al., OBG Management 2012).

Mesh exposure and erosion

Mesh exposure and erosion are known but infrequent risks of mesh sling surgery. Most often, mesh exposure into the vaginal wall is what is observed. It can be symptomatic or asymptomatic. When it does not bother the patient or her partner, it can be left untreated or

treated with estrogen cream. Otherwise the mesh can be revised in an in-office procedure, or where necessary, in the operating room. The incidence of vaginal mesh exposure is typically reported at 2% for midurethral slings. (Ford AA, Cochrane Review 2015, at 30; FDA Statement, March 27, 2013, Considerations About Surgical Mesh for SUI; Schimpf Table 3 (reporting rates between 1.4 and 2.2% for midurethral slings); Novara 2008 Table 6 (reporting exposure rates under 2%)).

There are patient characteristics which may increase the risk for mesh exposure. Clearly, there are some chronic medical conditions that interfere with wound healing and may make exposure rates more likely, such as diabetes. In addition, patients who fail to adhere to their vaginal restrictions in the immediate postoperative period are clearly more at risk for mesh erosions.

Erosion of the mesh into surrounding organs such as the bladder or urethra is very infrequent but can result in serious symptoms requiring prompt attention and likely a more complex surgical intervention. Of the over 30 studies of TVT with 24 month follow up addressed in Table 6 of the Novara 2008 meta-analysis, only 3 studies reported any incidence of bladder erosion and those were all under 2%.

XIV. ALTERNATIVE SAFER DESIGN

I am not aware – either based on my experience or my review of the medical literature- of an alternative material or alternative design to the TVT devices that reduces or eliminates their potential risks. Certain of plaintiffs' experts point to meshes such as Gynemesh PS, UltraPro, or PVDF as safer materials. Some experts claim that laser cut slings are safer than mechanical cut

slings, or vice versa. The fact is, there is no reliable published clinical data that supports any of their assertions.

I have searched for literature that comparatively studies tapes with mechanical cut vs. laser cut mesh and have found none, much less one that concludes that a particular method of cutting has a bearing on the safety of the device.

In addition, I have not been able to find reliable published studies demonstrating that Gynemesh PS, UltraPro or PVDF are safer materials than Prolene, or reduce, much less eliminate its risks. The study by Okulu et al. (2013) is no exception because it does not provide for a reliable comparison to TVT. TVT mesh was not even a comparator in the study. Rather the study compared Gynemesh PS, Vypro and Ultrapro in groups of only 48 patients. In addition, the techniques employed to implant these meshes in no way resemble the TVT approach: the slings were cut wide, rather than a narrow tape, and were implanted through an inverted “A” shaped incision rather than the two small 1 cm incisions required to implant TVT products. Moreover, the patients in these study groups still experienced exposure and at rates comparable exposure rates for TVT. In short, this study provides no credible basis to conclude that these materials would be safer than the Prolene mesh in TVT.

Nor does it provide any evidence that these materials would provide higher rates of effectiveness than TVT products. To the contrary, Ethicon had internally tested slings that were partially absorbable and experienced problems in benchtop and cadaveric testing related to the removal of the sheath that covers the mesh tape and the sterilization of the partially absorbable mesh. (See Report of K. Elbert, ETH.MESH.009922570-78).

Finally, plaintiffs' experts do not point to any alternative mesh or device that is actually FDA-cleared in the United States to treat SUI in women.

XV. PRODUCT WARNINGS

I have reviewed the IFUs for the TVT family of products, as well as professional education materials such as the TVT Surgeon's Resource Monograph and the TVT Secur Key Technical Steps booklet. It is my opinion that these documents accurately warn of the potential risks of the use of these slings as they are reported in the highest levels of medical literature which I have reviewed. They also appropriately take into consideration the risks that are commonly reported and known to trained pelvic floor surgeons who are the intended users of these devices.

My opinion is based on the following sources:

1. The 20 years of published medical literature on the TVT products. This includes Level 1 meta-analyses, systematic reviews, and randomized controlled trials, as well as numerous prospective studies following patients for over ten years for TVT and over five years for TVTO. These studies are discussed in detail in my TVT general report served in this MDL proceeding.
2. I have also reviewed and considered the FDA's "Blue Book Memo" which provides guidance on device labeling, and Ethicon's Standard Operating Procedure on Labeling (HMESH_ETH_11642462). These sources are informative, but do not weigh as heavily as the medical literature that assess the performance of these devices in thousands of women over years.
3. My training in urogynecology and pelvic reconstructive surgery as a resident.

4. My surgical experience in implanting approximately 2000 slings over the past 17 years and managing those patients' post-operative care, as well as treating patients who were implanted with slings by other doctors.

5. My years of experience in training residents, fellows and physicians in how to perform sling procedures. I have also been involved in postgraduate training sessions and cadaver labs which are focused on the indications, techniques, and complications of mid urethral slings.

6. My attendance at numerous local and national medical conferences, including the Annual Meetings of medical societies such as American College of Obstetrics/Gynecology. I have also participated in annual conferences of the American Association of Gynecologic Laparoscopists. At these meetings, I have observed numerous presentations regarding clinical studies of the TVT products by surgeons who have presented their findings, as well as with my informal interactions with my colleagues.

There is a particularly important paragraph in the TVT product IFUs stating that the IFU is not intended to be a comprehensive reference to surgical technique to treat SUI, and that the device should be used only by physicians trained in the surgical treatment of SUI and trained in the use of the device itself. This tells surgeons that Ethicon expects that the device users will be experienced and trained pelvic floor surgeons with a base knowledge of pelvic floor anatomy and risks of pelvic floor surgery in general. The IFUs repeat the warning about proper training on the device in the "WARNINGS AND PRECAUTIONS" section of the IFU. That section further advises physicians to avoid large vessels, nerves, bladder and bowel, and that "attention to patient anatomy and correct passage of the device will minimize risks." It also reinforces the

instructions for the surgical placement of the device in emphasizing: “Ensure that the tape is placed with no tension under the mid-urethra.”

The WARNINGS AND PRECAUTIONS section also warns of the possible risk of de novo detrusor instability which leads to overactive bladder, urgency and frequency symptoms, as well as (in the case of TVT-O) transient leg pain.

The Adverse Reactions section of the IFUs accurately lists the potential adverse events that are reported in the most reliable medical literature --- meta-analyses, RCTs, and long and medium term prospective observational trials – which are discussed in detail above in my report. It also warns doctors that if the sling is over-tensioned, this could result in obstruction of the lower urinary tract. The Adverse Reactions section provides as follows in all the TVT IFUs except for TVT Secur:

- Punctures or lacerations of vessels, nerves, bladder, urethra, or bowel may occur during needle passage and may require surgical repair.
- Transitory local irritation at the wound site and a transitory foreign body reaction may occur. This response could result in extrusion, erosion, fistula formation or inflammation.
- As with all foreign bodies, PROLENE mesh may potentiate an existing infection. The plastic sheaths initially covering the PROLENE mesh are designed to minimize the risk of contamination.
- Over-correction, i.e. too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction.

(TVT and TVT-O IFUs).

The TVT Secur IFU warns of these risks and adds a fifth bullet point warning that:

- Under-correction or incorrect placement may result in incomplete or no relief from urinary incontinence.

The medical literature that I have reviewed and my surgical experience does not demonstrate the cytotoxicity, degradation, chronic inflammation leading to complications and

other negative consequences that plaintiffs' experts claim. For that reason, they do not need to be included in the IFUs.

Other possible adverse events such as dyspareunia and pelvic pain are known risks of any surgery in the pelvic floor, including Burch and autologous slings. However, the medical literature I have reviewed does not typically demonstrate that such symptoms are associated with TVT brand slings unless there is surgical error in placement, over-tensioning, exposure (which the IFUs warn about), or concomitant surgeries.

I have also reviewed the 2015 revisions to IFUs of the TVT slings that are still on the market. The revisions did not provide previously unknown information to the medical community. A lot of the new language relates to general risks of pelvic floor surgery, or risks that are commonly known by trained pelvic floor surgeons. For example, it is not news to a trained surgeon that the device may not work, or may require additional surgeries to treat complications. Small percentages of failures have been reported in the medical literature for decades, as have reoperation rates.

The TVT Surgeon's Resource Monograph provides detailed information that supplements that provided in the product IFUs. Issued in 2001, the Monograph presents the best practices collected by a panel of 17 surgeons who were very experienced in TVT at that time. It provides detailed advice on patient preparation, anesthesia, incisions, device placement and post operative care. It also provides paragraphs of discussion on numerous potential adverse events including vaginal bleeding, retropubic hematoma, vaginal perforation, difficulty placing the needle, bladder perforations, voiding dysfunction and retention, injured urethra, urethral erosion, mesh protrusion or defective healing, vascular injuries, bowel perforations, de novo urge incontinence, infection of the mesh, urinary tract infection and device failure.

I am very familiar with the TVT Secur Key Technical Steps booklet. It is an excellent summary of the proper placement and tensioning of the TVT Secur device. It also nicely describes the relative and pertinent anatomy. This description is supplemented with excellent anatomical drawings. Furthermore, the booklet does an excellent job of teaching surgeons how to avoid complications and how to avoid improper placement of the sling. I used this booklet extensively when teaching residents and attending physicians the proper way to insert the TVT Secur device.

Finally, I have reviewed Ethicon's patient brochures for the TVT family of products . They appropriately perform that is intended for a patient brochure. They comprehensively discuss the medical condition of SUI, treatment options and potential risks. The risk discussion mirrors the IFU and is not misleading. While the brochure does not list every possible risk of surgery, that is not its purpose. Rather, it is the responsibility of the physician to have a comprehensive risk discussion with the patient that is tailored to the patient's individual needs.

XVI. SUMMARY OF OPINIONS

My opinions set forth in this report are made to a reasonable degree of medical certainty. My opinions are based on information and knowledge that I have acquired from my research and review of peer-reviewed medical literature, my education, training, personal experience in private practice, teaching, and discussion and interaction with other pelvic surgeons in professional activities and conferences. I reserve the right to modify or amend my opinions as I review more information.

1. The Gynecare TVT family of products are safe and effective and supported by 20 years of peer reviewed medical literature starting with the TVT Retropubic. This includes the

highest levels of evidence, including systematic reviews, meta-analyses and randomized controlled trials.

2. The benefits of these products far outweigh their risks in properly selected surgical candidates. Based on their performance in thousands of women as reflected in the medical literature, as well as my experience, they are not defectively designed.

3. The PROLENE® mesh that is used in the TVT products is a safe material for use as a midurethral sling to treat SUI. Polypropylene, as a mesh and as suture, has been used an implant for decades. The pore size is appropriate for proper tissue integration. Nor does the mesh typically result in infection.

4. The overall body of published clinical evidence (and my experience) does not demonstrate that PROLENE® mesh degrades in a way that is clinically significant to patients.

5. There is no reliable data to support the notion that mechanically cut mesh tapes are safer than laser cut implants, or vice versa. Whether to use a tape that is mechanically or laser cut is simply a matter of surgeon preference. Nor is there reliable clinical evidence to support the notion that particle loss is harmful to patients.

6. A chronic foreign body response is not an adverse event. It is an expected and desired result of the placement of any surgical implant which reflects the human body's histological process of incorporating a foreign body. The peer reviewed medical literature I have reviewed does not demonstrate that this process generates adverse clinical outcomes when the sling is implanted according to correct technique.

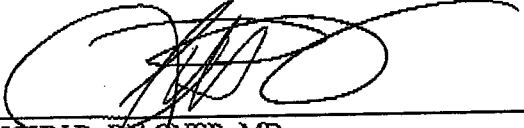
7. There is no reliable evidence in the published medical literature of an alternative design to the TVT products, or to Prolene mesh, that reduces or eliminates the potential risks of these devices.

8. The possible risks of the TVT family of products are appropriately described in their Instructions for Use, the patient brochures for the TVT family of products, and in Ethicon's professional education materials. These materials properly reflect the risks that are reported in the high-level medical literature and appropriately account for the common knowledge of trained specialists.

Expert Rates

My work on this matter has been or will be billed as follows: \$350 per hour for records review, preparation of expert reports, and consultation; \$2500 per half day of deposition or trial testimony; and \$5000 for full day of deposition or trial testimony.

Dated: January 31, 2017


JOHN R. WAGNER, MD